

CSIRO Molecular & Health Technologies

Celesta Fong



CSIRO in Australia



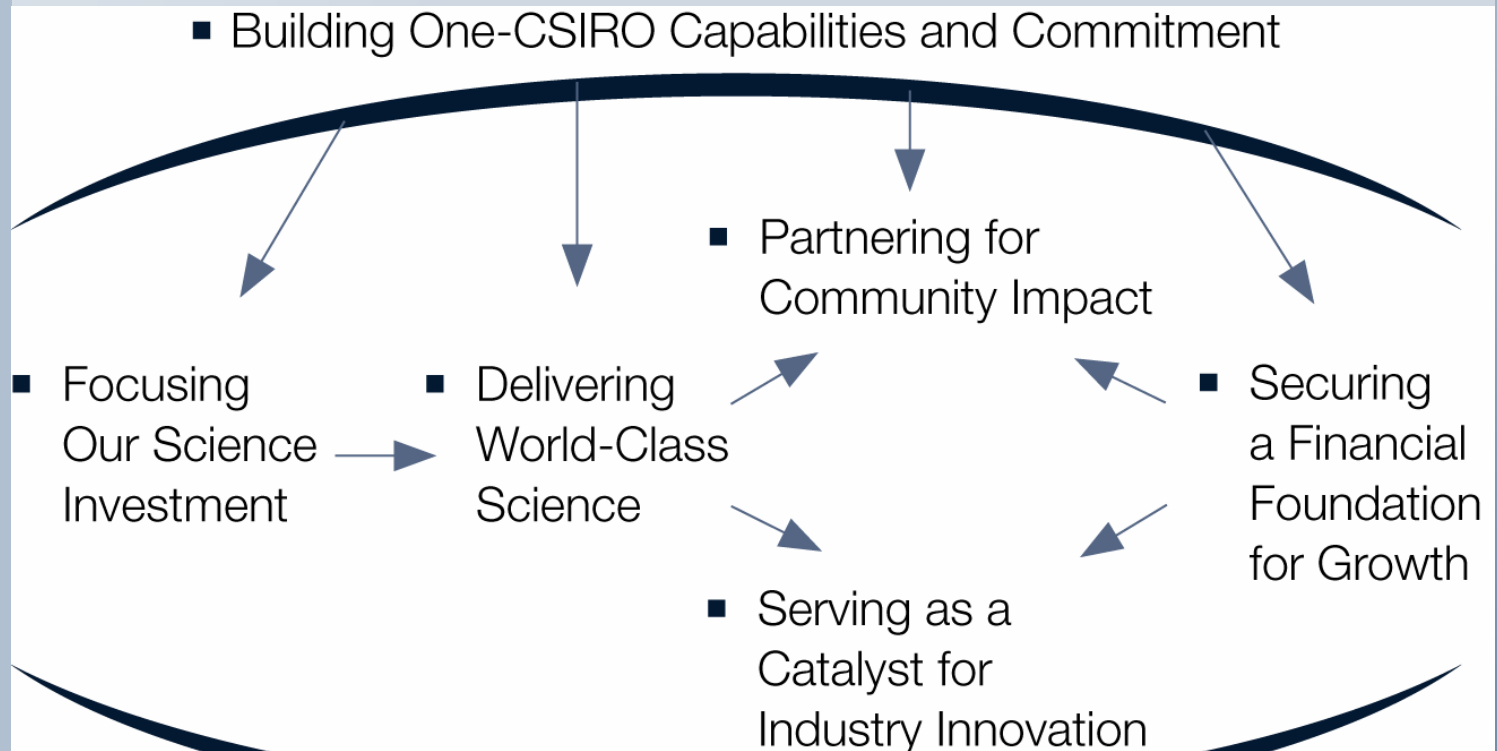
CSIRO is a Federal Government Agency. Its annual budget of over \$900 million comes from the Federal Government and external sources.

CSIRO's research spans agriculture, food, environment, manufacturing industry, minerals, energy, information technology, health, infrastructure and services.



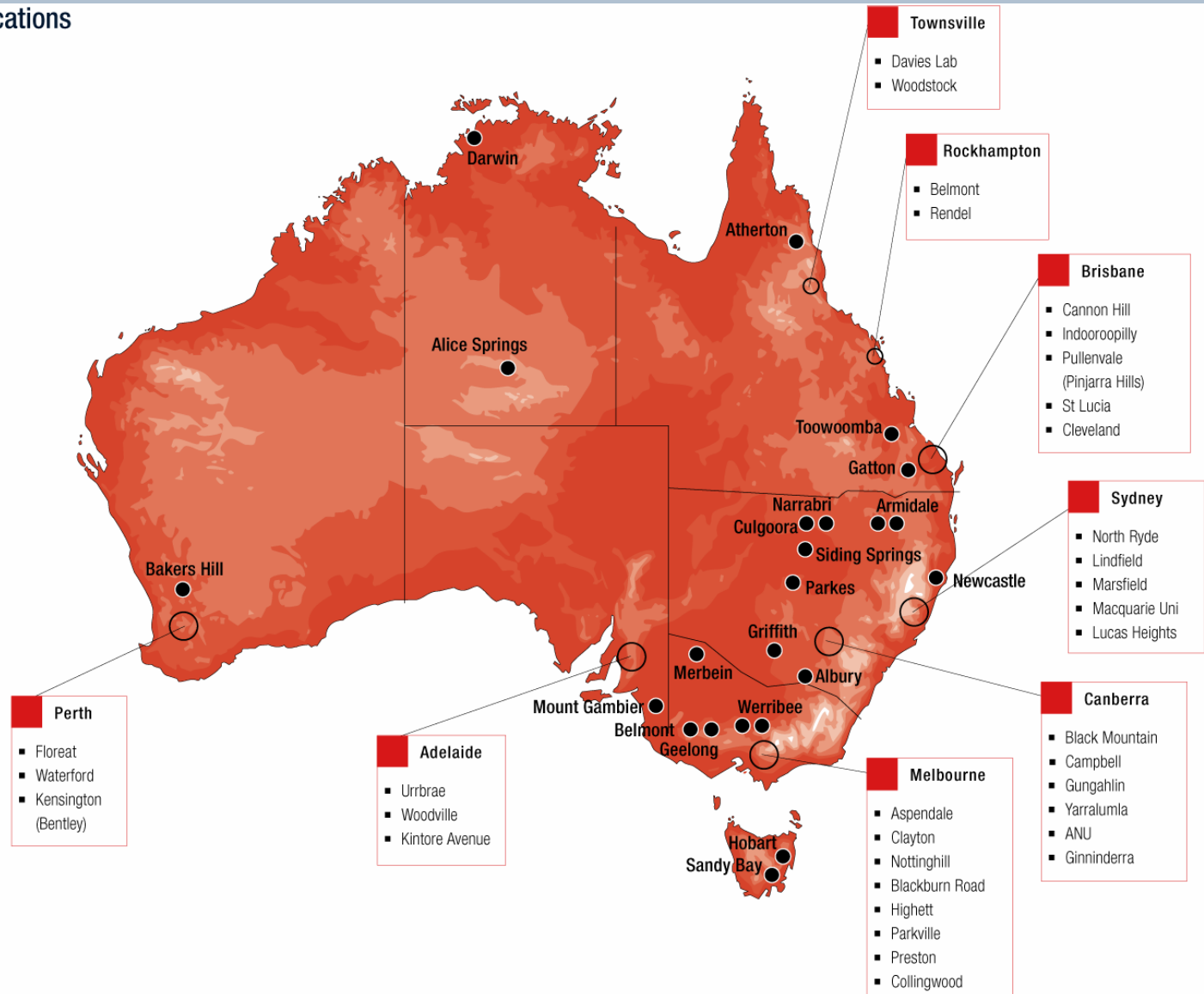
CSIRO's Mission Statement & Strategy

“By igniting the creative spirit of our people, we deliver great science and innovative solutions for industry, society and the environment.”



CSIRO across Australia

CSIRO locations



CSIRO Molecular & Health Technologies: CMHT

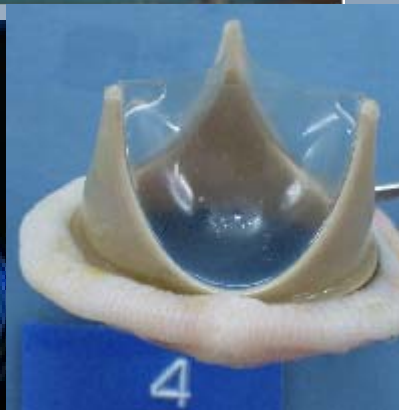

- 4 Laboratories; 320 staff; multidisciplinary skills base
 - Melbourne
 - Clayton: synthetic chemistry, polymers, materials
 - Parkville: protein chemistry
 - Sydney (North Ryde): molecular and cellular biology
 - Adelaide: toxicology, animal models
- Access to Major Facilities
 - Australian Synchrotron (Clayton)
 - OPAL reactor (Menai)




CMHT Themes

- Biomaterials and Regenerative Medicine
 - The development and application of novel biodegradable and bioactive biomaterials suitable for the repair, replacement and regeneration of diseased or damaged body parts.
- Electroactive Materials
 - The development of new platform technologies for polymer electronics.
- Australian Biotech Growth Partnerships
 - Supporting Australian biotech SMEs, particularly in the agricultural and health biotech sectors.
- **Nanobiotechnology-Sensing & Delivery**
 - **Development of smart nanomaterials with in-built biological functionality for targeted bioactive delivery and diagnostics**

CMHT Achievements



dr manny noakes with dr peter clifton

the CSIRO total wellbeing diet

- the weight loss program that can actually work
- a healthy eating plan for life

the new scientifically proven diet for Australians

CSIRO and CMHT Research Focus

CSIRO's research is focused and delivered in three major areas:

- Priority-driven core research
- National Research Flagships
- **The Emerging Science Initiative (ESI)**

Hierarchical Material Structures: Creating Novel 3-D Porous Particulate Systems by Developing Combinatorial and High-Throughput Methodologies



NIST-CSIRO Collaboration

High-through put characterisation of multicomponent complex systems (phase behaviour)

In the quest to rationally design advanced materials the challenge remains to deconvolute the relationship between structure, composition and function.

NIST-CSIRO Collaboration

High-throughput characterisation for surfactant phase behaviour

- Phase diagrams contain the complete information on the thermodynamic and kinetic phase behaviour of a system in the most compact form.
- Phase diagrams of complex systems are, extremely scarce, largely due to the huge amount of tedious and painstaking work required to collect the data.
- A key scientific challenge is to reduce the time required to generate a phase diagram from weeks to a day or less.

CMHT-Philosophy for Mesophase Development

Devise Novel Surfactant Structures based on empirical literature observation and semi – empirical theory

Synthesise

Re-engineer structures

**Screen Phase Behaviour
Temperature ranges, phases etc.**



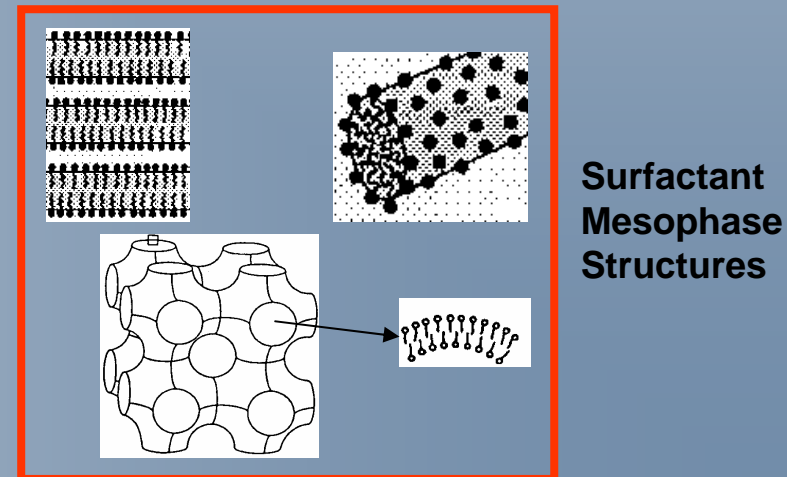
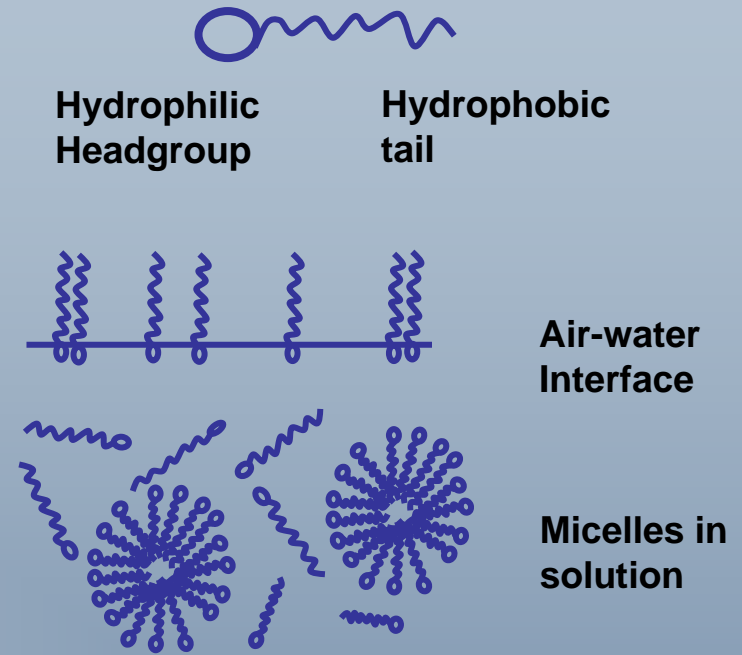
Surfactant Self Assembly

Surface active agents
are amphiphiles

They Spontaneously
accumulate at interfaces,
lowering interfacial tension

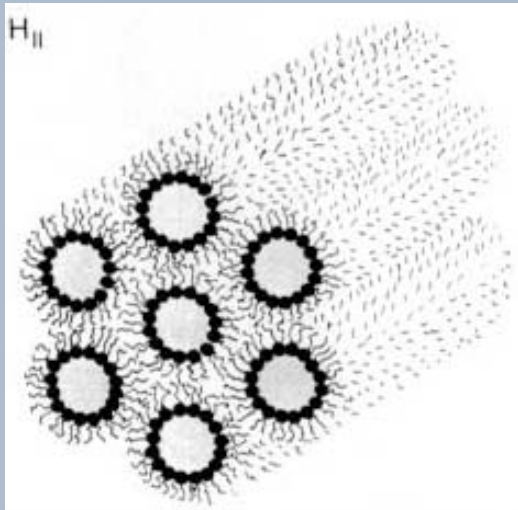
At higher concentrations, they
self assemble in solution to form
spherical aggregates: micelles

Further complex structures may
form depending on molecular
geometry and environmental
conditions (temperature,
concentration, salt etc.) =
“Surfactant Phase Behaviour”

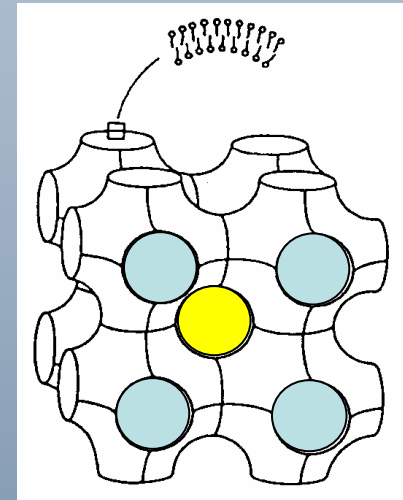


Mesophase Systems

Inverse Hexagonal Phases



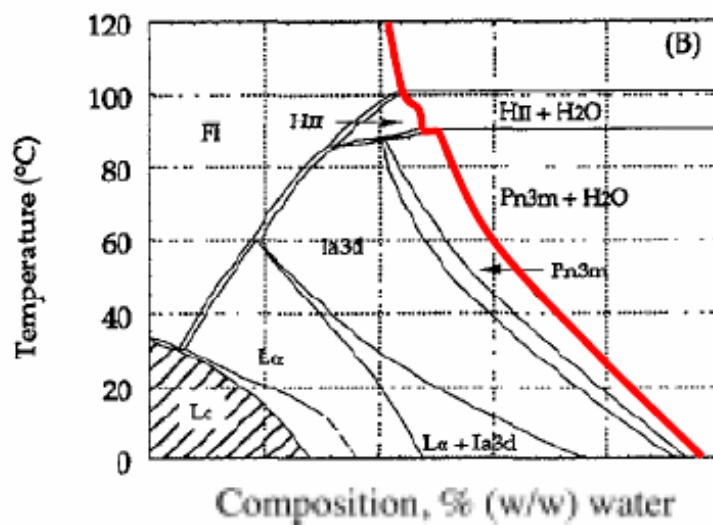
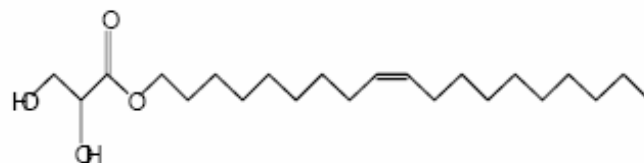
Inverse Cubic Phases



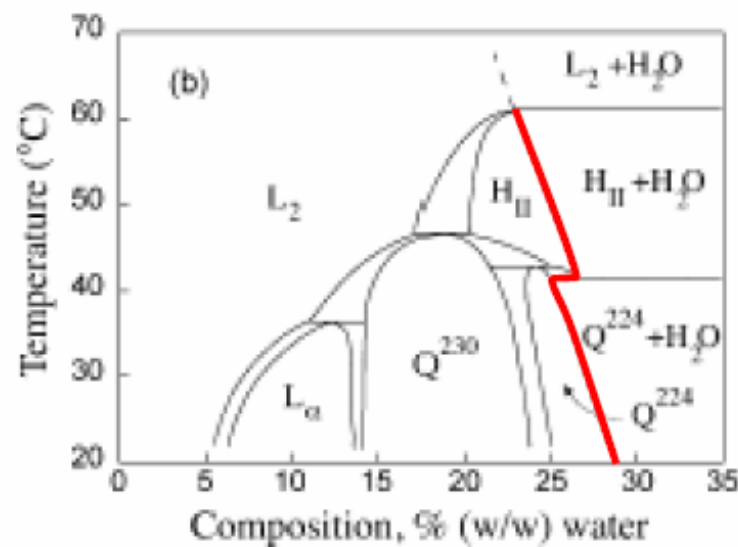
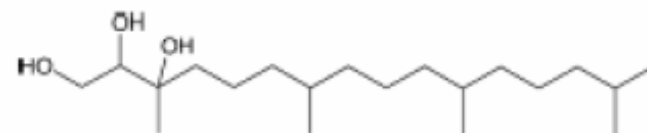
- ✓ Bicontinuous networks
- ✓ Containment of aqueous and/or non polar species
- ✓ Unique 'nanoenvironments' for solubilization
- ✓ High Tortuosity for release
- ✓ 3-D high capacity for solutes (cf. liposomes)
- ✓ Stability against dilution & rupture proof

Dilutable Phase Behaviour

Glycerol Monooleate (Monoolein)



Phytantriol



Qui and Caffrey, *Biomaterials*, 21, 2000, 223-234

Barauskas and Landh, *Langmuir*, 19, 2003, 9562-9565

Inverse Phases: Wedge Shaped Molecules

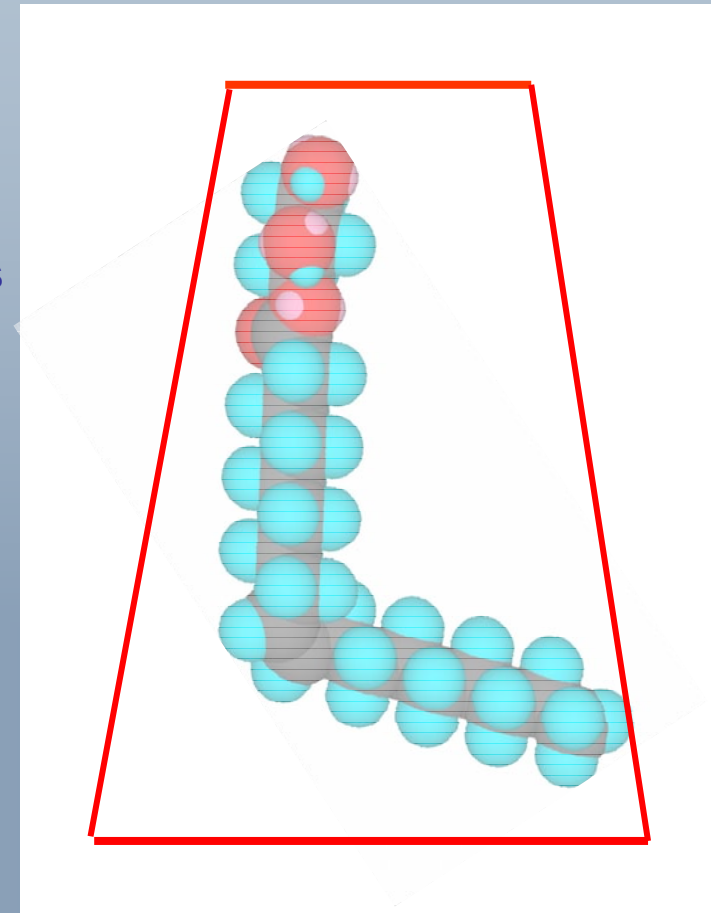
Inverse phases not normal phases are stable to dilution (excess water).

To obtain high (-) interfacial curvature wedge shaped molecules with relatively small head group area and large chain cross sectional area are required.



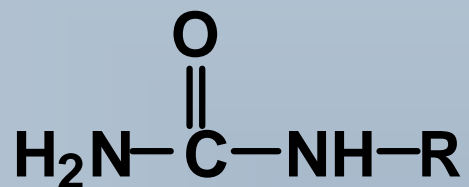
Strategies for increasing CPP include :

- branching (positional isomerism)
- unsaturation
- multiple hydrophobe attachment

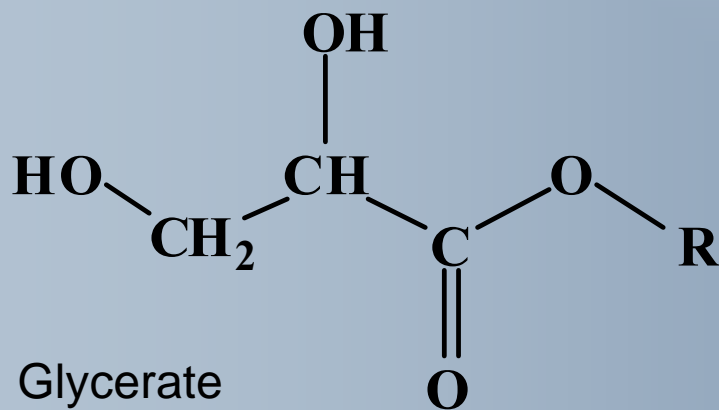


Monoolein

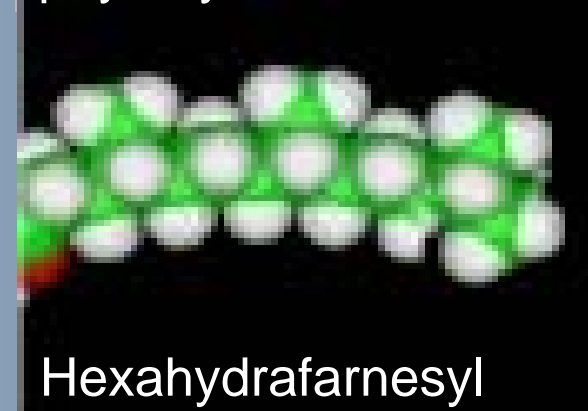
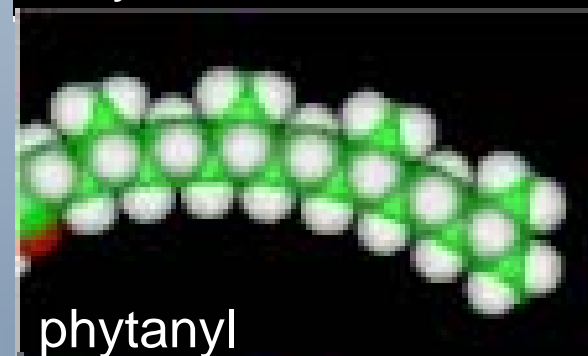
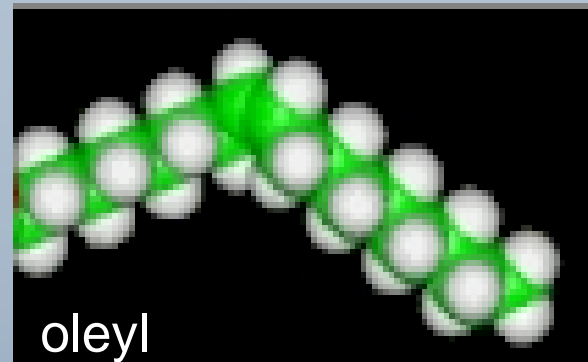
Engineered Mesophases



Urea



Glycerate



Fong and Drummond et. al. Chem. Mater., 18, 594-597, 2006

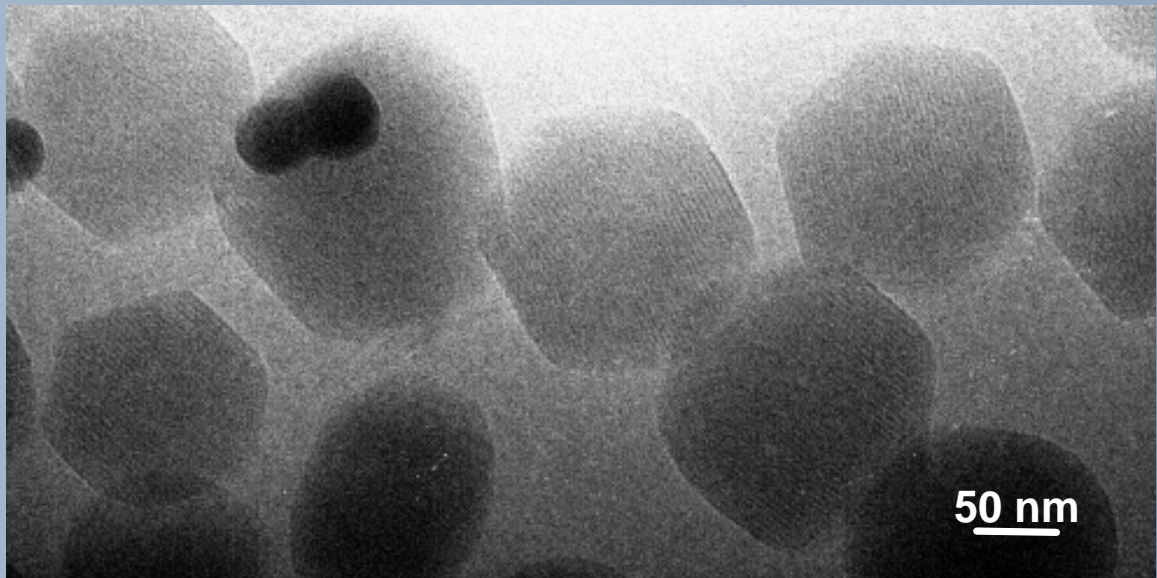
Fong and Hartley et. al. Aust. J. Chem., 58, 683-687, 2005

Boyd, B.B., et. al. PCT WO 2004/022530A1

Engineered Mesophases

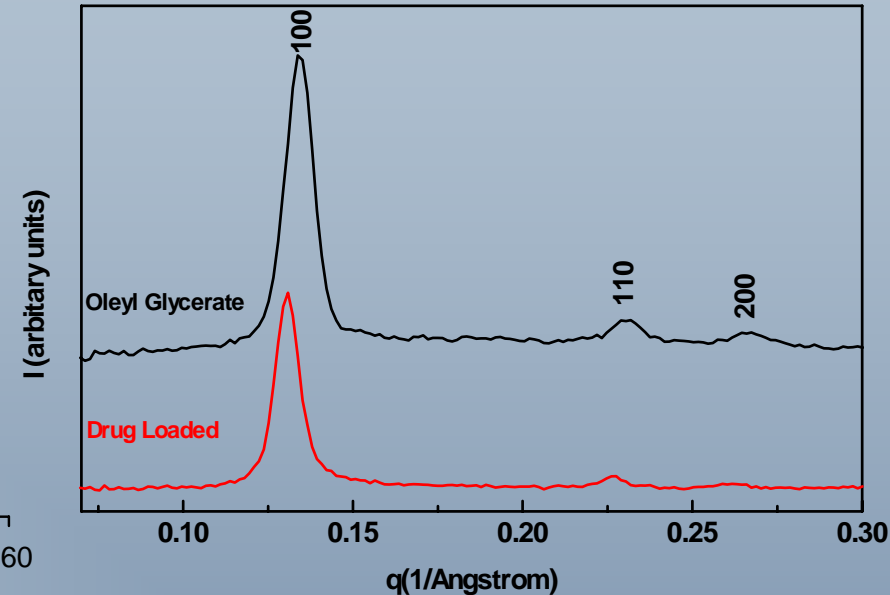
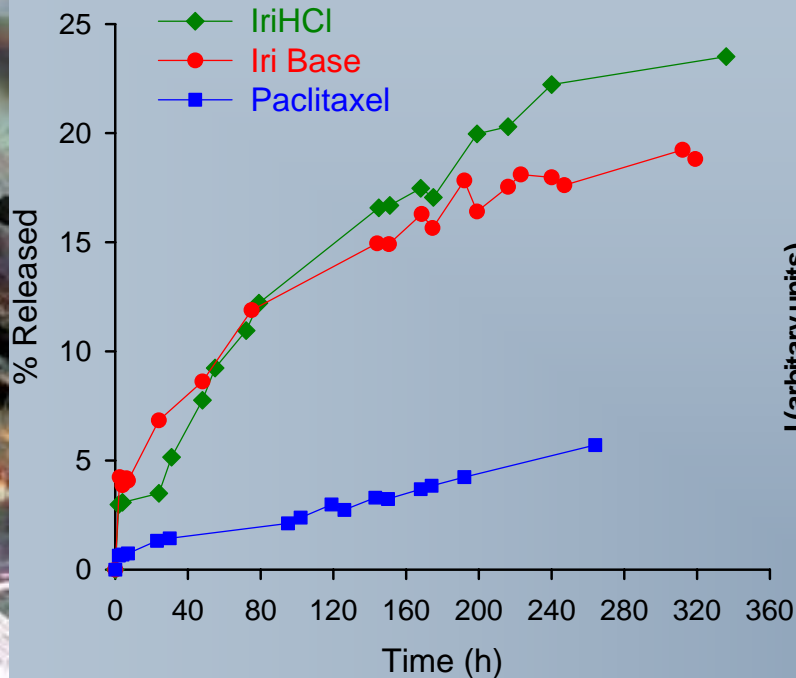


LPM oleyl glycerate



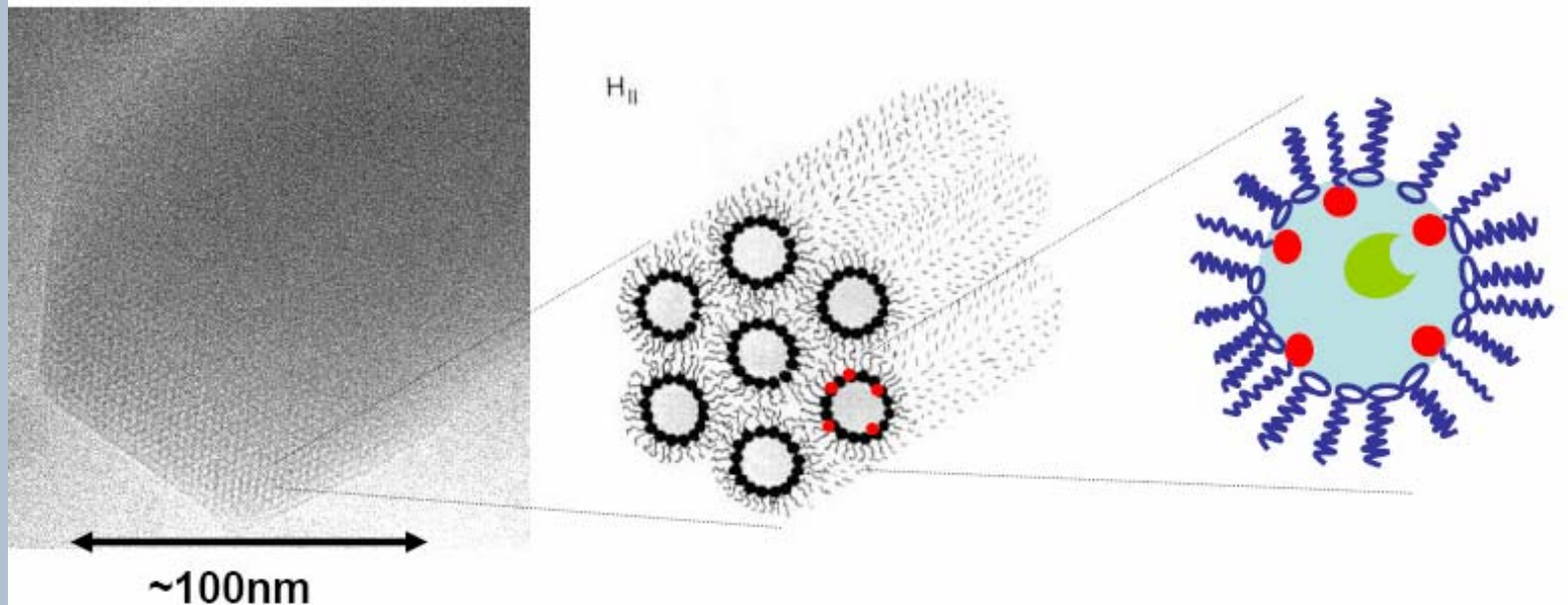
Colloidosomes

Drug Release from Engineered Mesophases



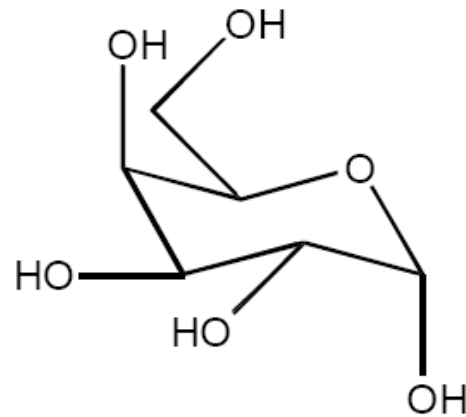
- Sustained release of anti-cancer agents irinotecan base/HCl (hydrophilic) and paclitaxel (lipophilic) from bulk phase of Oleyl glycerate. This suggests potential for depot formulations.
- Encapsulation does not alter phase behaviour

Polyvalent Mesophases

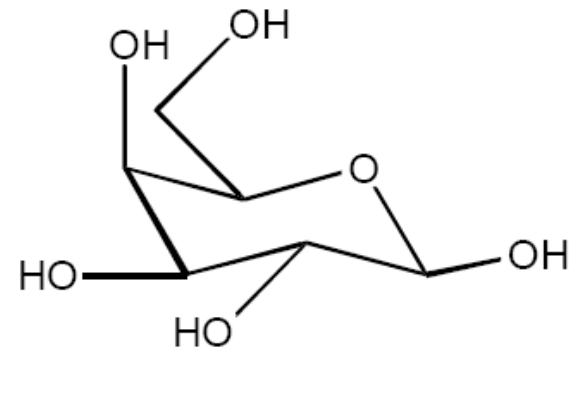


- Polyvalent ligands incorporated as co-surfactants to 'mop up' receptor sites to block adverse cellular interaction (eg. ricin)
- High density of surface binding sites
- In diffusion and entrapment within mesophase

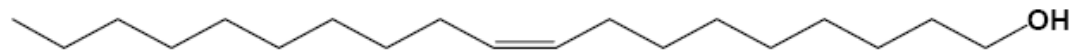
Polyvalent Mesophases for Ricin Remediation



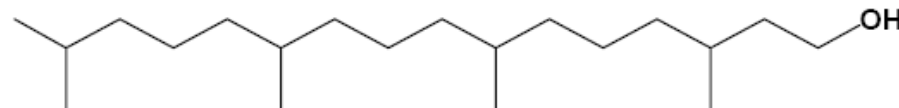
α -Galactose



β -Galactose



Oleyl Alcohol



Phytanol

Surfactant Mesophases for Bioaffinity Separations

Composition	% Ricin Removed
Phytantriol (Control)	8.6
<i>Inverse Hexagonal Mesophase Mixtures</i>	
40% Galactose-6-phytanoate/ Phytanyl glycerate	12.2
50% Phytanyl β -1-galactoside/ Phytanyl glycerate	22.4
20% Oleyl α -1-galactoside / Oleyl Glycerate	39.6
<i>Inverse Cubic Mesophase Mixtures</i>	
40% Galactose-6-oleate/Oleyl glycerate	40.5
40% Oleyl α -1-galactoside / 60% oleyl glycerate	80.3
40% Oleyl β -1-galactoside/Oleyl glycerate	85.1
40% Phytanyl β -1-galactoside / 60% Phytantriol	90.3
30% Oleyl α -1-galactoside / phytantriol	91.3

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CSIRO Molecular & Health Technologies

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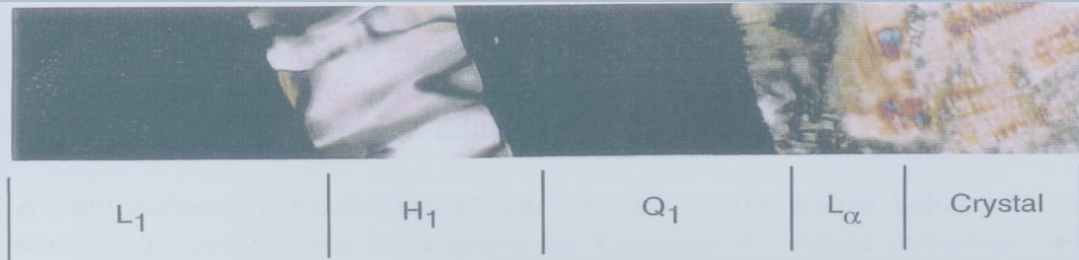
CSIRO: People & Infrastructure

- CSIRO ranks in the top 1% of world scientific institutions in 11 of 22 research fields
- 60% of our staff hold university degrees
 - >1800 doctorates
 - > 430 masters' degrees
- Citations per publication are 30% above world average
- More than 160 companies are based on CSIRO intellectual property

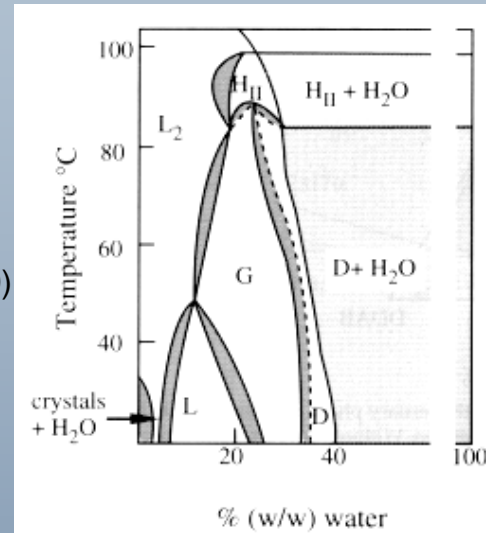


Physico-Chemical Characterisation

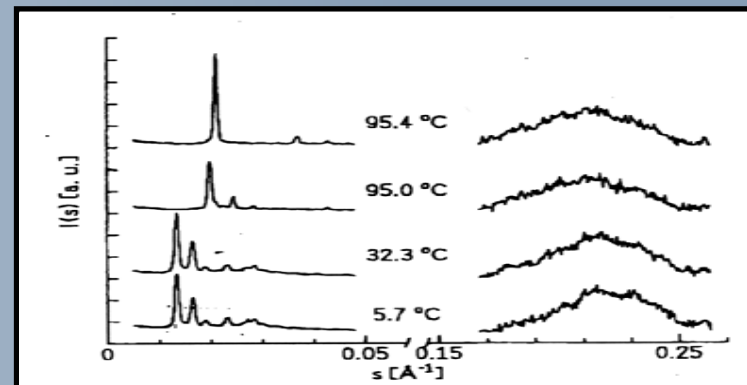
Water penetration scans: Light polarising microscopy

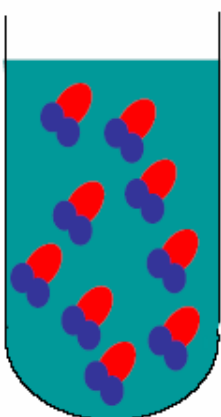


(Boyd, PhD Thesis, 1999)

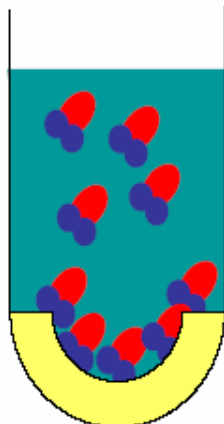


Small Angle Scattering -SAS

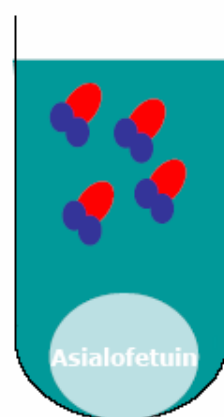




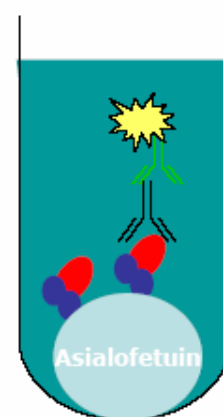
Known [Ricin]



Incubate with
Mesophase



Take supernatant,
incubate with
asialofetuin



Wash and probe
with ELISA,
Correlate wrt. [ricin]
calibration curve

**Goat-anti-rabbit
IgG - AP**

Rabbit Anti-ricin

Dawson et. Al.,
J. Appl. Toxicol. **19**, 307–312 (1999)

Bicontinuous Cubic Phases

